REMARKS

By this amendment claims 1-5, 7, 13-16 and 21 are canceled. Claims 6, 8-12, 17-20 and 22-25 are pending. No issue of new matter arises. Entry of the amendment and reconsideration and withdrawal of all pending rejections in each of the multiple parts thereof are respectfully requested.

Rejection under 35 U.S.C. §103(a)

At page 4, the Office Action rejected claims 1-25 as allegedly "being unpatentable over Citron et al., 1998, Neurobiology of Diseases, 5: 107-116 in view of St. George-Hyslop et al., US Patent 6,395,960, patented May 28,2002, Ishii et al., 1997, Neuroscience Letters, 228: 17-20, Borchelt et al., 1997, Neuron, 19: 939-945, and Xia et al., 1997, The Journal of Biological Chemistry, 272: 7977-7982."

The rejection is further characterized in the paragraph bridging pages 5 and 6 with the following statement:

> "Citron et al. teach that kidney cells were stably transfected with APP695 and a PS1 double mutant and that these cells had higher levels of Abeta42 than cells that have single mutations in PS1 (Citron et al. page 111, 2nd col., under Abeta42 Effects of the PS1 Mutations M146L and L286V Are Additive). Given this teaching, Citron et al. teach that presenilin mutations have a systemwide effect of Abeta42 production and can therefore be studied in a peripheral cell line (Citron et al., page 112, 1st col. under Discussion). Citron et al. also teach that cells that predominantly make the Abeta42 protein will be useful for localizing the subcellular sites of Abeta42 production and understanding the way in which mutant presenilin alters APP proteolysis. By additional manipulations, it would be possible to generate cell lines and transgenic animals which would produce almost exclusively Abeta42 (Citron et al. page 115, 1st col., 1st parag.)."

And at page 5, lines 6-8 from bottom the Office Action alleges: "It is noted, that the art at the time of filing teaches that peripheral cells that express mutant PS1 exhibit apoptosis (St. George-Hyslop et al., col. 20, 3rd parag.)." Applicants respectfully submit that such statement cannot be found in a review of columns 19 and 20. Accordingly, an affidavit under 37 C.F.R.

§1.104(d)(2) is respectfully requested explaining how the personal knowledge of the Examiner arrived at this conclusion from column 20, 3rd paragraph.

As mentioned above, claims 1-5, 7, 13-16 and 21 are canceled. Applicants respectfully traverse this rejection with respect to the remaining claims.

Applicants respectfully submit that no *prima facie* case of obviousness has been established.

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. **MPEP §2143.**

At least the methods of claims 6, 8-12, 17-20 and 22-25 cannot properly be said to be *prima facie* obvious. The primary reference is discussed above. The secondary references are not alleged to remedy noted deficiencies of the primary reference.

First, there is no suggestion or motivation, either in the applied references themselves or in any knowledge generally available to one of ordinary skill in the art that is cited in the Office Action, to modify the reference or to combine reference teachings to "detect[] compounds intended for the treatment of neurodegenerative diseases".

Second, there is no indication of a reasonable expectation of success. The references are chiefly concerned with producing Abeta42 and provide no expectation that cells designed for production would apoptose. Simply protein producing cells would not be expected to apoptose as cells must be viable for protein production. Secondary references are alleged to teach specific mutations. These teachings cannot be said to remedy the deficiencies of Citron.

Finally, the prior art reference (or references when combined) cannot properly be said to teach or suggest all the claim limitations. Making a transgenic animal as a source of peripheral cells for transgenic monitoring is not suggested in the applied references. For example, Citron, teaches production of "double transfected cell lines" for studying Abeta42 production, See, e.g.,

page 108, column 2, top paragraph. There is no suggestion to produce a transgenic mammal and then to use that mammal for "detecting compounds intended for the treatment of neurodegenerative diseases . . . in a renewable peripheral tissue." Accordingly, Applicants respectfully submit that none of the three criteria necessary to establish a *prima facie* case of obviousness are present. Dependent claims are patentable over the prior art for at least the same reasons that the claim(s) from which they depend are patentable over the prior art. Reconsideration and withdrawal of this rejection of all pending claims are respectfully requested.

Conclusion

In view of the above amendments and remarks, Applicants respectfully submit that the application is now in condition for allowance and request prompt issuance of a Notice of Allowance. Should the Examiner wish to suggest additional changes that might put the application in even better condition for allowance, the Examiner is requested to contact the undersigned at the telephone number listed below.

Fees

The Commissioner is hereby authorized to charge any fee required for added claims and any additional fees that may be needed to Deposit Account No. 18-1982.

Respectfully submitted,

Dated: December 17, 2009

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